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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,718	01/26/2004	Rustem F. Ismagilov	7814-95	2568
757 7590 10/09/2007 BRINKS HOFER GILSON & LIONE P.O. BOX 10395 CHICAGO, IL 60610			EXAMINER GAKH, YELENA G	
			ART UNIT 1797	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/765,718

Applicant(s)

ISMAGILOV ET AL.

Examiner

Yelena G. Gakh, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-74 is/are pending in the application.
- 4a) Of the above claim(s) 64-74 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 16-21, 35-37 and 45-48 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date See Continuation Sheet.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :09/13/04,
11/01/04, 04/14/0~~5~~, 07/05/0~~5~~, 07/28/0~~5~~, 05/25/0~~6~~, 11/17/0~~6~~, 06/18/0~~7~~.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-63, drawn to a method for crystallization, classified in class 436, subclass 4.
 - II. Claims 64-65, drawn to a method for indexing a component, classified in class 436, subclass 56.
 - III. Claims 66-74, drawn to a capillary tube, classified in class 422, subclass 245.1.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are the method for crystallization and the method for indexing a component in a plug of a microfluidic substrate. Although both inventions relate to microfluidic methods, they are totally different processes having different modes of operation and different effects, and require different search.

Inventions I-II and III are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the processes can be performed in open microchannels, rather than in capillaries, and also the capillary is a conventional capillary in a pipette with e.g. a protein solution, when the pipette is filled with solution plugs separated by air bubbles.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

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2. During a telephone conversation with Yuezhong Feng on 09/27/07 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-63. Affirmation of this election must be made by applicant in replying to this Office action. Claims 64-74 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Double Patenting

3. Applicant is advised that should claim 7 be found allowable, claim 8 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The method of crystallization the way it is recited in the claim is not enabled by the specification. According to the specification, introducing a plug-fluid into a carrier-fluid, which is immiscible with the plug-fluid, results in forming a plug of the plug-fluid in the carrier fluid. According to claim 1 there are three

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independent fluids introduced into the carrier fluid, which all form their own plugs in the channel. There is no way for them to mix with each other, since they are all separated by the immiscible fluid. This makes the method of forming crystal of the crystallization target un-enabled, because formation of the crystal requires intermixing a solution comprising a precipitant and a solution comprising a crystallization target. The claim does not recite any possible ways for such intermixing to take place.

Claim 2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method, which comprises merging specific plugs from two channels, e.g. the plug comprising the precipitant and the plug comprising the crystallization agent, does not reasonably provide enablement for the method, in which such merge does not take place. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. If the merge occurs for the plugs comprising the same components (e.g. the precipitant or the crystallization agent), since the combined plugs are separated by immiscible fluid, no mixing between the reagents, and therefore no crystallization, will take place.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

While the carrier-fluid is defined in the specification as the fluid immiscible with any of the plug-fluids, the examiner suggests the Applicants to introduce the definition “immiscible” for the carrier-fluid in the body of the claims in order to clearly define, as to how plugs are formed from the plug-fluids, without the necessity of referring to the specification. This does not narrow the scope of the claims, since the specification provides exactly such definition for the carrier-fluid.

The recitation of claim 1 is not quite clear. Are all three plug-fluids introduced separately into the plug-forming region of the first channel? Is this region different from the rest of the channel? It is also not clear, why it is pressure applied to plug-fluids that causes formation of the

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plugs, rather than introducing the plug-fluids into the immiscible carrier-fluid? Is the pressure applied periodically to the plug-fluids? The recitation is not clear. Further, it is unclear from claim 1, how the crystallization target forms the crystal when the steps recited in the claim are performed. It is further not clear, if the claim recites the same solvent for all plug-fluids. Also, it is not quite clear, which solvent is meant for the second plug-fluid, which comprises water? Is this an additional solvent?

From claim 2 it is not apparent, whether the recited first, second and third plug-fluids are different from those recited in claim 1, since they are recited with an indefinite article “a”. It is also not clear, if the application of pressure to the plug-fluids introduced into the first and second channels is anyhow synchronized? Is it constantly applied? It is not apparent, as to how the merge of plugs can occur, if there is no synchronized formation of the plugs in two channels and their transporting to the merge point. Moreover, if such synchronization occurs, it is not apparent, whether the plugs from the first and the second channels that are merging are the same, i.e. comprising the same compounds? If they are the same, it is not clear, as to how crystallization can take place, since crystallization requires mixing two different plugs.

From claim 3 it is not apparent, as to how the crystallization is prevented in the plug of the first plug type, which comprises both the precipitant and crystallization target? Further, claim 3 is confusing as to which specific embodiment it recites, with a plurality of combinations of introducing plugs of the first and second type in different plug-forming regions of the first and second channel. Furthermore, it is not apparent, as to what is the difference between the first, the second and the third plug-forming regions, and where these regions are located - in both channels, in one of the channels? Claim 3 is unclear and indefinite.

Claim 6 is not apparent, as to how the solvent can be transferred from one plug into another, if the plugs are separated by the carrier fluid immiscible with the solvents of the plugs? It is also not clear, if “a solvent” of claim 6 is anyhow related to “a solvent” of the parent claims? If it is the same solvent, the article “the” should be used instead.

It is not apparent, as to what is the difference between the first and the second plug-forming regions, and therefore it is not clear, as to what is the difference between recitations of claims 9 and 10.

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Claim 13 is confusing. Which specifically plug-forming region out of three is meant in the claim? Also, how the second carrier fluid can separate plugs, which are already introduced into the first channel?

Claim 15 recites introducing the carrier-fluid into the substrate - this appears to be different from introducing the fluids into the channels of the substrate of the parent claims. The examiner suggests rewriting the claim as reciting "into the channel(s)".

Examiner's Note. In order to provide antecedent basis for the limitations in all dependent claims, indefinite article "a" should be replaced with "the" in all claims, where appropriate.

From claim 16 it is not clear, why the plug-fluid does not replace the carrier-fluid in a channel thus forming a column of the plug-fluid instead of the plug, if the pressure is applied continuously upon introducing the plug-fluid?

The limitation "at least one of the flow rates" recited in claims 18-19 does not have an antecedent basis.

From claim 22 it is not apparent, whether the concentration gradient is formed within one plug, or along several plugs, with each plug having a specific concentration?

Claim 23 recites mixing, which is not mentioned in the parent claims.

Claim 24 has the same problem as claim 15. Besides, the subject matter of claim 24 is very confusing. How is it possible that "the concentration of a first component in the plug of one plug-type provides a correlative and quantitative measure of a second component in an adjacent plug"? What one has to do with the other? The recitation does not seem to be meaningful.

It is not clear from claim 25, how "a marker" is related to the precipitant or the crystallization target, which are the major components of the plugs? It is the marker for what?

It is unclear from claim 26, which plug-fluid comprises a salt, since a salt can be a co-precipitant, and also it is not clear, how the plug with the crystallization target can comprise the salt?

Claims 40-41 seems to contradict the definition of the "carrier fluid" provided in the specification, which is supposed to be immiscible with the plug-fluids, at least one of which comprises water.

8. The claims as originally filed are written in such unclear and indefinite language that the examiner cannot apply the prior art to the pending claims in any meaningful manner.

The examiner respectfully requests the Applicants to clarify the subject matter of the pending claims and invites the Applicants for a telephonic interview if they consider this assisting the prosecution of the instant application.

9. Upon further consideration of the claims the examiner found several restrictable groups of species and respectfully requests the Applicants to elect species from each of the groups for further examination:

Group I: pressure is applied continuously (claim 16); pressure is halted after the plugs are formed Claim 17).

Group II: flow rates are constant relative to each other (claim 18); flow rates are varied relative to each other (claim 19).

Group III: plug-fluid is introduced at a constant rate (claim 20); they are introduced at a variable flow rate (claim 21).

Group IV: carrier-fluids comprise: an oil (claim 35), a fluorinated compound (claim 36), a surfactant (claim 37), FMS-121 (claim 45), PFP (claim 46), PFP and PFO (claim 47), PFO (claim 48).

Group V: the substrate comprises a material, which allows water evaporation from the plugs (claim 60), and which does not allow water evaporation from the plugs (claim 63).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

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Conclusion

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. *Titomanlio et al. (AIChE Journal, 1990)* teach "capillary experiments of flow induced crystallization of HDPE" (title); ***Garcia-Ruiz et al. (Acta Crysta., 1994)*** - the closest prior art - demonstrate "investigations on protein crystal growth by the gel acupuncture method" (title); ***Sugiura et al. (Langmuir, 2001)*** - the closest prior art - teach "interfacial tension driven monodispersed droplet formation from microfabricated channel array" (title); ***Garcia-Ruiz et al. (J. Crystal Growth, 2001)*** - the closest prior art- teach "a super-saturation wave of protein crystallization" (title); *Ng et al. (J. Struct. Biol., 2003)* disclose "protein crystallization by capillary counter-diffusion for applied crystallographic structure determination" (title).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

9/28/2007



YELENA GAKH
PRIMARY EXAMINER